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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,436	08/13/2001	Mitra Tadayoni-Rebek	0942.5300001/RWE/AGU	6227

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EXAMINER
LUKTON, DAVID

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 05/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,436	TADAYONI-REBEK ET AL.	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-20,39 and 41-52* is/are pending in the application.

4a) Of the above claim(s) *17,20 and 44-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,19,39,41-43,51 and 52* is/are rejected.

7)☒ Claim(s) *18,49 and 50* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/7/05 has been entered.

Pursuant to the directives of the response filed 11/7/05, claims 16, 17, 19, 20, 39, 50 have been amended. Claims 16-20, 39, 41-52 remain pending. Claims 44-47 remain withdrawn from consideration. In addition, claims 17, 20 and 48 are now withdrawn from consideration, in view of the amendment to claims 17 and 20. The elected specie was a specific marker molecule, and not a "marker molecule composition" that required multiple repetition of labeling and ligation processes in order to obtain.

Applicants' arguments filed 11/7/05 have been considered and found persuasive in part. The previously imposed rejections under 35 U.S.C. § 112, 1st and 2nd paragraphs are withdrawn. Claims 16, 19, 39, 41-43, 51, 52 are rejected; claims 18, 49 and 50 are objected to because of their dependence on rejected claims.

Claims 16, 18, 19, 39, 41-43, 49-52 are examined in this Office action.

✧

The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Canne (USP 6,326,468).

As indicated previously, Canne discloses a peptide ligation method in which a peptide bearing an N-terminal cysteine is reacted with another peptide bearing a C-terminal thioester group to form a larger peptide. Reaction schemes are summarized, e.g., in figures 1, 16, 20 and 21. As is evident, the coupling process can be performed more than once. Also suggested (col 14, line 60+) is that the "first peptide segment" or the "incoming peptide segment" can be used in excess.

In response to the foregoing, applicants have amended the claims to require that the peptide be labeled with a "chromophore". Applicants have also argued that absorption of a compound in the UV range is not a sufficient condition for the compound to be a chromophore. But applicants also recognize that fluorophores are chromophores. This comes very close

to an admission that tryptophan is a chromophore. Whether or not applicants agree that they have admitted that tryptophan is a chromophore, the fact is that tryptophan **is** indeed a chromophore, and so the rejection is maintained.

✧

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Kent (USP 6,307,018).

As indicated previously, Kent discloses (e.g., figure 1) a coupling procedure in which a "peptide 1" bearing a thioester group is reacted with a "peptide 2" bearing an N-terminal sulfhydryl moiety. As indicated above (the §103 over Canne), dipeptides, tripeptides, tetrapeptides (etc.) that contain Trp qualify as chromophores. Kent does not disclose a peptide that contains tryptophan, but the there exist millions of peptides that contain such. Surely, the reference provides no reason to <u>avoid</u> peptides that contain tryptophan. If the disclosed method is to be useful at all, it would have to be useful for tryptophan-containing peptides. There are countless biologically active peptides which contain tryptophan and for which the peptide chemist of ordinary skill would have reason to synthesize.

The rejection is maintained.

✧

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Kent (USP 6,476,190).

As indicated previously, Kent discloses (e.g., figure 1) a ligation procedure in which a C-terminal thioester of a "first" peptide is reacted with a "second" peptide, wherein the second peptide bears an N-terminal bromoacetyl group. The result is a new peptide which itself contains a thioester bond (at the point of ligation). At least one of the disclosed peptides contains tryptophan (see e.g., col 6, line 53).

The rejection is maintained.

✧

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Canne (USP 6,326,468) in view of any of the following: McKernan (USP 5,698,521) or DeBaryshe (USP 5,713,364) or Kittrell (USP 5,562,100).

The teachings of Canne are indicated above. Canne does not teach that tryptophan is fluorescent. The secondary references, however, teach this. Relevant passages are as follows:

- McKernan discloses (col 19, line 38+) that tryptophan absorbs in the UV.
- DeBaryshe discloses (col 1, line 62+) that tryptophan is fluorescent.
- Kittrell discloses (col 5, line 31+) that tryptophan is fluorescent.

Thus, a dipeptide or tripeptide (or tetrapeptide) subsequence that contains Trp will be a fluorescent label. The claims are thus rendered obvious.

✧

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Kent (USP 6,307,018) in view of any of the following: McKernan (USP 5,698,521) or DeBaryshe (USP 5,713,364) or Kittrell (USP 5,562,100).

The teachings of Kent were indicated previously. Kent also discloses peptide sequences that contain at least one of Phe, Tyr and Trp. In addition, the process disclosed in the reference is intended for any peptide; there are countless peptides known that contain at least one of the three amino acids in question. Kent does not teach that tryptophan is fluorescent. The secondary references, however, teach this. Thus in preparing the peptide precursors (that Trp), one is meeting step (a) of the instant claims. And Kent clearly teaches the ligation step. Thus, the claims are rendered obvious.

✧

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Kent (USP 6,476,190) in view of any of the following: McKernan (USP 5,698,521) or DeBaryshe (USP 5,713,364) or Kittrell (USP 5,562,100).

The teachings of Kent were indicated previously. Kent also discloses peptide sequences that contain Trp. In addition, the process disclosed in the reference is intended for any peptide; there are countless peptides known that contain at least one of the three amino acids in question. Kent does not teach that tryptophan is fluorescent. The secondary references,

however, disclose this.

Thus, in preparing the peptide precursors (that contain Trp), one is meeting step (a) of the instant claims. And Kent clearly teaches the ligation step. Thus, the claims are rendered obvious.

✧

Claims 16, 19, 39, 41-43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Nishikata (USP 5,917,012) in view of Canne (USP 6,326,468).

Nishikata discloses (col 3, line 20+; col 5, line 17+) peptides that contain two chromophores. The chromophore can be e.g., an amino acid bearing coumarin or an N^{ϵ}–(dinitrophenyl)lysine. Though Nishikata discloses compounds that would qualify as "marker molecules" in accordance with the claimed invention, he does not disclose the claimed *method of making* the marker molecule. Canne discloses methods of making peptides. Advantages of the claimed method can be found, e.g., at col 3, line 55+. Thus, it would have been obvious to one of ordinary skill to use the Canne method to make the Nishikata peptides.

✧

Claims 16, 19, 39, 41-43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Nishikata (USP 5917012) in view of Canne (USP 6,326,468), further in view of Sakakibara (USP 4,138,394) or Houghten (USP 5,763,193).

The teachings of Nishikata are indicated above; the teachings of Canne were indicated

previously.

Nishikata does not characterize dinitrobenzene as being a "chromophore". However, this is disclosed in the tertiary references (Sakakibara: col 2, line 40; Houghten: col 30, line 14).

Thus, the claims are rendered obvious.

✧

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Canne (USP 6,326,468) in view of Siani (USP 6,844,161).

The teachings of Canne were indicated previously. Canne does not disclose that tyrosine is a chromophore. Siani discloses (col 14, line 4) that tyrosine is a chromophore, but Siani does not disclose the claimed method.

Thus, it would have been obvious that in preparing a tyrosine-containing peptide according to the method of Canne, the requirements of the claims are met.

✧

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Kent (USP 6,307,018) in view of Siani (USP 6,844,161).

The teachings of Kent were indicated previously. Kent does not disclose that tyrosine is a chromophore. Siani discloses (col 14, line 4) that tyrosine is a chromophore, but Siani does not disclose the claimed method.

Thus, it would have been obvious that in preparing a tyrosine-containing peptide according to

the method of Kent, the requirements of the claims are met.

✧

Claims 16, 19, 39, 42, 43, 51, 52 are rejected under 35 U.S.C. §103 as being unpatentable over Kent (USP 6,476,190) in view of Siani (USP 6,844,161).

The teachings of Kent were indicated previously. Kent does not disclose that tyrosine is a chromophore. Siani discloses (col 14, line 4) that tyrosine is a chromophore, but Siani does not disclose the claimed method.

Thus, it would have been obvious that in preparing a tyrosine-containing peptide according to the method of Kent, the requirements of the claims are met.

✧

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON, PH.D.
PRIMARY EXAMINER